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Dosimetric Comparison of Fractionated Stereotactic Radiotherapy Plans With And Without Flattening Filter Beams of 6 MV And 10 MV Beams

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ABSTRACT

Introduction: It is necessary to understand the importance of different energies in Fractionated Stereotactic Radiotherapy (FSRT) plans for better outcome. The study objective is to compare FSRT plans with Flattening Filter (FF) and Flattening Filter Free (FFF) beams.

Material and Methods: Twelve patients with primary Brain Metastasis (BM), were selected and given 25 Gy in five fractions for which 6FF beams were angled in double arc. The Planning Target Volume (PTV) and Organs at Risk (OARs) were assessed using dosimetric indices after each plan was replanned with 6 FFF, 10 FF, and 10 FFF energies. Treatment time (TT) and Monitor Units (MUs) were also compared. Additionally, we compared portal dosimetry for dose agreement across all plans using the gamma analysis criterion.

Results: PTV parameters of created plans showed better values when compared to 6 FF plans, where the most significant is with FFF plans which include D98%, D80%, D2%, D50% and Dose Gradient Index values of 6FFF plans. Among OARs, the most significant is the V10 value of (Brain-PTV) as (46.77±43.9) and maximum dose values of optic chiasm, brainstem, and left lens in 6FFF plans. Among technical parameters, the 6FFF plan showed significant TT value of (3.06±1.0) with p-value 4.13E-05. Better gamma analysis passing rates were achieved with FFF beams.

Conclusion: Linear accelerator-based FSRT delivery of BM using 6 FFF beam results in better dosimetric indices, OAR sparing, fastest treatment delivery, and energy conservation with reduced peripheral and out-of-field dose for higher treatment modalities like Rapid arc.

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Introduction

Malignant tumours that have spread to the brain from other regions of body such as lung, urinary tract is called brain metastases (BM) [1]. Fractionated stereotactic radiotherapy (FSRT), is used to treat BM and can be performed using a variety of technologies, including the CyberKnife, Gamma Knife, helical TomoTherapy, and linear accelerators [2]. For patients with oligometastatic cranial illness, Stereotactic Radiosurgery (SRS) and FSRT has emerged as an effective therapy option with few side effects [3]. Patients with 1-4 BM with a survival time of more than three months are presently advised to receive SRS or FSRT alone over whole-brain radiation therapy (WBRT) albeit SRS has a lower risk of neurocognitive adverse effects and a higher quality of life [4]. By introducing the Flattening Filter Free (FFF) in Linac, we could eradicate the problem of prolonged-time consumption treatment, which lasts up to 45 to 60 minutes for SRS with a conventional linac setup [5]. Flattening Filter (FF) and FFF beams both exhibit identical penumbra areas in scanned profiles, but the dose fall-off with lower values is more apparent for FFF, considerably effecting less field dosage for FFF beams.

With this study, we hope to better understand how FF and FFF beams at 6MV and 10MV energies perform in brain FSRT treatment regimens and assess their dosimetric qualities. Dosimetric parameter data for FFF modality have been documented in a number of publications at locations including the prostate, liver, and lungs; however, research describing the effect of a 10MV FFF beam on BMs are very uncommon, making ours both unique and useful. [6]. Previous studies on SRS cases with FFF reported that when the dosimetric comparison of FF and FFF beams was carried out, it showed similar dose distributions for FF and FFF plans [7]. Additionally, in contrast to previous studies using intensity-modulated radiotherapy (IMRT)

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technology, our research used rapid arc technology FSRT plans for this evaluation since it has been said that the volumetric modulated arc therapy (VMAT) plan with FFF beams is favourable for its potentials, including lower collimator scatter, greater dose rate, less head leakage, and reduced out-of-field dosage to the patient, as well as the fact that the prolonged delivery time it requires per fraction for IMRT may deteriorate the treatment accuracy due to the intra-fractional motion of the patient [8-9]. Each patient's Rapid arc FF and Rapid arc FFF plans have been optimised using the same gantry arcs, collimator angles, optimization goals, and priority to eliminate any potential for bias in the study. The study is novel as it assessed both 6MV and 10 MV beam FSRT plans based on dosimetric parameters of PTV and OARs and additionally evaluated its portal dosimetry results and technical parameters.

Materials and Methods

After getting clearance from the institution's ethics council, 12 individuals aged 35 to 75 with a diagnosis of solitary brain metastasis were chosen to participate in the research. All of the patients were simulated in the head-first supine position with a 3-point hybrid head mask to keep their heads immobilized. A planning computed tomography (CT) scan was done at 1mm slice intervals, and the results were sent to the Treatment Planning System (Eclipse TPS version 15.06). Since CT with contrast enhancement specifies the extracranial disease state, it was decided to merge the CT images with Magnetic Resonance Image (MRI) scans obtained from the same perspective in order to better localize the tumour and the Organs at Risk (OARs). However, MRI scans with contrast enhancement may count BM and evaluate the patient's anatomical presentation. An initial Planning Target Volume (PTV) was contoured around the Gross Tumour Volume (GTV) with a 2mm margin in all dimensions, using data from prior FSRT trials and the geometric accuracy provided by intra-fractional mobility (ICRU 91). Axial CT slices were also used to delineate OARs and designate an additional amount of healthy tissue outside of the PTV.

For this tumour, 25Gy in 5 fractions was given (5Gy per fraction). Depending on the tumour's location, rapid arc designs either used full arc or partial arc with noncoplanar and non-overlapping beams of up to ±15% couch rotation, moving in a clockwise and anticlockwise pattern to achieve sharp dose fall-off in the plans. With the aim of achieving PTV coverage of V100% > 95%, all plans were normalized at low isodose and with small or no margin for beam penumbra at the edge of the target in order to improve the dose fall-off outside the target volume and spare nearby critical organs which were optimized for 6MV X-ray beams using the Photon Optimizer (15.6.05) algorithm. The dose was also calculated using the Anisotropic Analytical Algorithm (AAA) at a 2.5mm calculation grid size. Dose limitations for OARs were established in a manner analogous to the optic chiasm: Dmax < 20Gy; (Brain-PTV): V12 <20 cc, V12 <25 cc; Brainstem: D0.1< cc 20 Gy, Dmax <25 Gy; Left and Right Optic nerve: D0.2 cc< 23 Gy, Dmax <25 Gy; Left and Right Eye: Dmax< 25 Gy; Left and Right Lens: Dmax <10 Gy where Dmax- Maximum dose, D0.1cc- Dose to 0.1cc of volume, D0.2cc- Dose to 0.2cc of volume. Based on the Dose Volume Histogram (DVH), tumour coverage, and OAR dosage, the plans were evaluated and approved. Each session of Rapid arc on Truebeam STx, which included a 6-dimensional couch and a tiny multi-leaf collimator with 120 leaves, required the daily placement of the patient and confirmation of their location using cone beam computed tomography (CBCT).

Each plan (base plan) was copied and replanned for our study with 6FFF, 10FF, and 10FFF energies. The dose rate set was 600MU/min for 6FF and 10FF energies, whereas, for 6FFF and 10FFF, it was 1200MU/min. Except for dose rate, all other machine and optimization parameters were kept identical for all the plans to avoid bias. The four plans were compared using the DVH analysis, tumour volume coverage, OAR doses, and technical attributes. In addition to the Conformity Index (CI), Conformity Number (CN), Coverage Index (COVI), and Dose Gradient Index (DGI), other dosimetric parameters were examined for plan evaluation [10]. The conformity of the high dosage to the objective is assessed using the parameter CI ($1 \leq CI < 1.2$).

CI = Prescription Volume / PTV volume

The CN was determined to evaluate dose compliance, as it considers both tumour volume and healthy tissue irradiation. The ideal value of CN is 1 and is defined as;

CN = (TVpi /TV) x [TVpi/Vpi]

TVpi is Target Volume within the prescribed isodose volume, TV is the tumour volume and Vpi is the volume of prescribed isodose volume. The COVI, which is defined as TVpi/ TV, is discussed; a value of 1 is optimal. The DGI is computed as follows, with an ideal value of 1, where PI is the volume of the recommended isodose and D50% is the volume of 50% of prescribed isodose volume. A lower DGI indicates larger dose gradients in the vicinity of the target. When comparing PTVs, we also recorded their mean dose, D2%, D98%, D50%, and D80%. There were maximum doses, average doses, and suitable values of volume receiving xGy recorded for all OARs specified. Values for the mean dose, V5, and V10 (volume at 5 and 10 Gy, respectively) are recorded for normal tissue. To study the efficacy of alternative distribution techniques, information on technical aspects such as Monitor Units (MUs) and Treatment Time (TT) was collected.

Portal dose image prediction (PDIP) was used to establish the dosage distribution for each trial participant (Varian Medical Systems, Pala alto, USA). A gamma index criterion of 3% dose difference and a 3mm distance to agreement were used in all plans to assess

the dose agreement between the PDIP and the portal dosimetry measurement.

SPSS 26.0 was used to analyse the data. To determine whether the data were normally distributed in light of this, we used the Shapiro-Wilk test. Means and standard deviations served as representation for the continuous data. To identify statistically significant differences between pairings, paired t-tests were utilized. The assumption of statistical significance was made when the p-value was below 0.05. [11].

Results

Figure 1 displays the isodose curve distributions for a single patient over all plans. The DVH comparison of a patient's PTV and OARs in all plans is shown in Figure 2. The gamma results of all plans of the patients under study is shown in Figure 3.

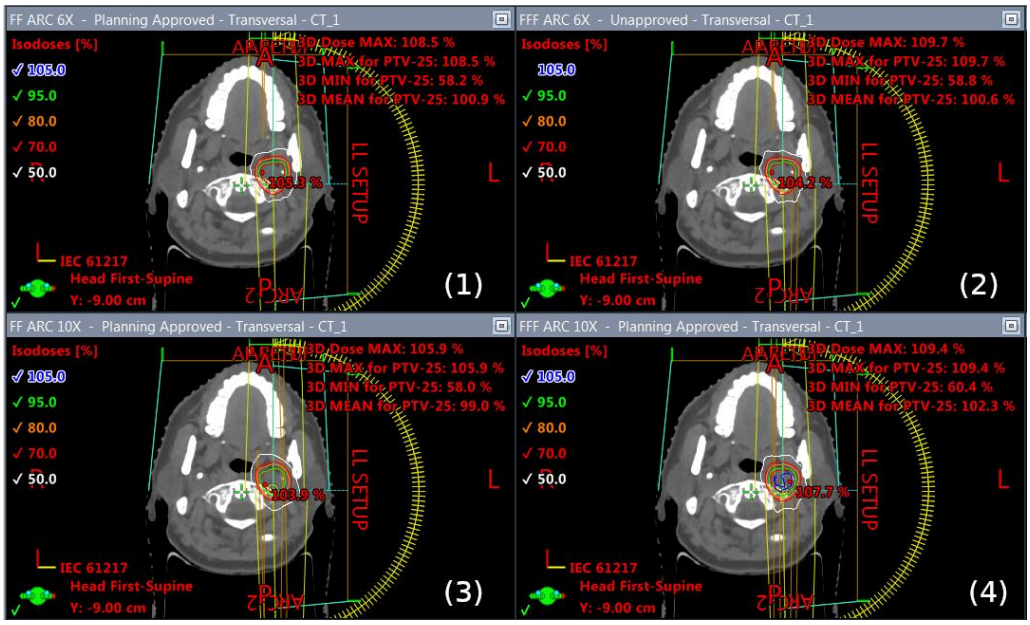

Figure 1. The isodose curve distributions of (1) 6FF, (2) 6FFF, (3) 10FF and (4) 10FFF plans under study for a single patient

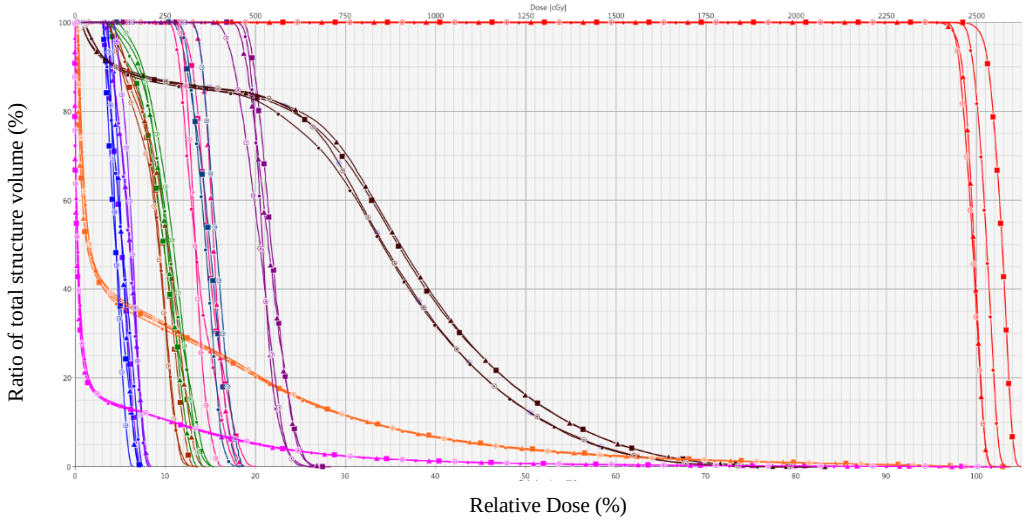

Figure 2.The Dose Volume Histogram comparison of Planning Target Volume and Organs at Risk of all plans for a single patient

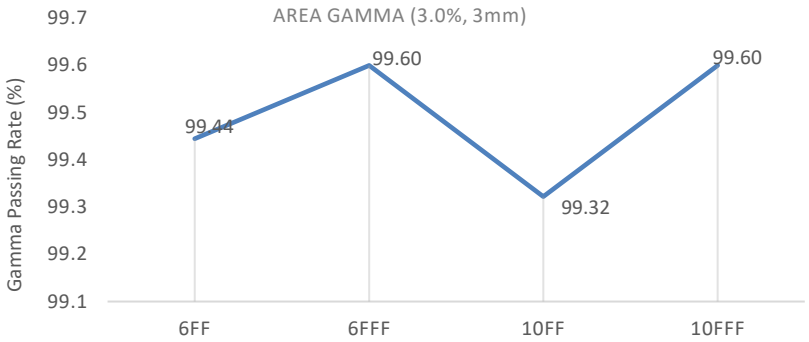

Figure 3. Gamma results of all plans of the patients under study is shown

Table 1. Planning Target Volume parameters of all plans under study along with p-values

PARAMETERS	6X		10X		p-value		
	FF	FFF	FF	FFF	6FFF	10FF	10FFF
MeanDose	25.09±0.55	25.28±0.92	24.87±0.65	25.67±0.68	0.345	0.128	0.003
D2%	25.92±0.62	26.20±0.67	25.78±0.67	26.59±0.67	0.004	0.083	0.000
D98%	23.60±0.85	23.65±1.16	22.91±1.43	23.68±1.52	0.807	0.065	0.822
D50%	25.20±0.54	25.39±0.60	25.02±0.62	25.82±0.64	0.048	0.100	0.001
D80%	24.78±0.44	24.92±0.57	24.43±0.72	25.23±0.76	0.255	0.085	0.044
CI	1.10±0.07	1.12±0.09	0.95±0.18	1.15±0.13	0.563	0.019	0.168
CN	0.80±0.06	0.80±0.07	2.19±4.35	1.57±2.71	0.290	0.317	0.364
COV I	0.94±0.06	0.94±0.06	1.15±0.87	1.15±0.74	0.862	0.452	0.348
DGI	0.27±0.05	0.35±0.22	0.33±0.27	0.36±0.28	0.298	0.485	0.292

FF- Flattening Filter; FFF- Flattening Filter Free

Table 2.Organ at Risks parameters of all plans under study along with p-values

OARs	Parameters	6X		10X		p-value		
		FF	FFF	FF	FFF	6FFF	10FF	10FFF
OPTIC CHIASM	MAX DOSE(Gy)	2.95±3.2	2.35±2.28	2.42±2.4	2.32±2.3	0.347	0.644	0.579
BRAIN-PTV	V12(CC)	37.8±35.4	35.15±30.1	26.56±34.0	28.53±30.3	0.228	0.082	0.158
	V10(CC)	50.74±51.5	46.77±43.9	41.91±50.6	41.12±46.5	0.203	0.150	0.158
BRAINSTEM	D0.1CC(Gy)	11.18±6.5	12.76±7.9	11.34±6.6	12.09±7.8	0.270	0.086	0.213
	MAX DOSE (Gy)	13.54±7.1	12.66±8.3	13.32±7.2	14.05±8.3	0.249	0.553	0.459
LT ON	D0.2CC(Gy)	1.15±1.1	1.23±1.3	1.13±1.2	1.15±1.2	0.403	0.862	0.881
	MAX DOSE(Gy)	1.52±1.3	1.55±1.4	1.54±1.4	1.56±1.5	0.437	0.800	0.717
RT ON	D0.2CC(Gy)	1.14±1.2	1.16±1.2	1.21±1.2	1.15±1.1	0.280	0.141	0.792
	MAX DOSE(Gy)	1.71±1.5	1.71±1.5	1.75±1.0	1.67±1.5	0.883	0.310	0.513
LEFT EYE	MAX DOSE(Gy)	1.21±1.1	1.23±1.1	1.29±1.2	1.27±1.1	0.556	0.151	0.191
RIGHT EYE	MAX DOSE(Gy)	1.80±1.2	1.71±1.2	1.73±1.0	1.65±1.1	0.235	0.335	0.245
LEFT LENS	MAX DOSE(Gy)	0.65±0.59	0.64±0.61	0.64±0.65	0.64±0.65	0.824	0.868	0.859
RIGHT LENS	MAX DOSE(Gy)	0.69±0.56	0.69±0.59	0.72±0.60	0.65±0.52	0.874	0.482	0.256
HEALTHY TISSUE	V5(CC)	5.48±4.2	5.17±3.5	1.95±1.4	1.95±1.4	0.203	0.005	0.007
	V10(CC)	1.89±1.6	1.81±1.3	1.82±1.4	1.82±1.4	0.379	0.094	0.417
	MEAN DOSE(GY)	0.89±0.5	0.86±0.4	0.87±0.4	0.86±0.4	0.228	0.070	0.166

FF- Flattening Filter; FFF- Flattening Filter Free

Table 3. Technical parameters of all plans along with p-values

PARAMETERS	6X		10X		p-value		
	FF	FFF	FF	FFF	6FFF	10F	10FFF
MU	1148.53±162.1	1297.57±307.1	1155.03±246.2	1206.69±275.4	0.055	0.903	0.328
TT	4.38±1.1	3.06±1.0	4.19±0.9	3.01±1.0	4.14E-05	0.212253	7.79E-05

MU- Monitor Units; TT- Treatment Time; FF- Flattening Filter; FFF- Flattening Filter Free

From Table 1 of PTV parameters, the significant values are mainly noted for D98%, D80%, D2% and D50% values of 6FFF and 10FFF as well as the DGI value of 6FFF.

Among OARs in Table 2, the most significant results is with FFF plans which includes the maximum dose values of brainstem and left lens; V10 and mean dose values of healthy tissue in 6FFF plans. Similarly, the maximum dose values of right optic nerve, right eye and right lens; V5 value of healthy tissue of 10FFF plans. Due to the large distance between the PTV and some OARs, the dosage exposure to these OARs is seemed to be insignificant.

From Table 3 of technical parameters, it is observed that the MUs have increased and the TT has reduced to a very minimum in 6FFF and 10FFF plans. In support of this conclusion, Zhuang et al., results had greater MUs due to the modulation needed to deliver uniform doses in large volume tumours and lower TT values with increased dose rate for SRS in FFF mode [12-13].

Discussion

We chose to focus on FSRT patients for our research of brain metastases, despite the fact that FSRT was recommended for BM by the German Society for Radiation Oncology (DEGRO) and that the dosage prescription should be based on the volume size and closeness to other OARs.[14]. The other highlight of our study selection is that here the dose fraction is as per a publication in which they proposed hypofractionated radiation treatment (SFRT) for reducing the risk of late side effects of BM like radio necrosis and one among such different dose prescription schedule is 25Gy in 5 fractions for delivering good results based on clinical outcomes and tolerability [15]. Moreover, here the selected FSRT cases are treated on Linear accelerator unit which overweighs it from other related studies as it is narrated that there is high interest and demand for the Linac-based SRS and FSRT applications [16].

Our study is very much significant in aspects of all its results compared to others which stated that FFF beams showed similar dosimetric parameters and plan quality with no OAR sparing when compared to the FF beams [17]. Nevertheless, in all sectors of dosimetric and technical parameters studied, our results showed significant differences which prioritizing FFF from FF.

Among the PTV parameters, all parameters showed their significant values in specific plans compared with the base plan 6FF except mean dose, among which the most prominent is the 6FFF plan with its significant p-values both in 6FFF and 10FFF which is contradicting those of stieler et al., who found no difference in plan quality between FF and FFF.[18].

In the case of OARs parameters, except for the V12 value of (Brain-PTV), all other OAR parameters showed their most significant and reduced dose values in 6FFF and 10FFF plans. Plans created in FFF mode for SRS are said to be of equivalent quality to those created in FF mode, but with less radiation exposure to healthy brain tissue.[19]. Our study findings are a beneficial effect of FFF to reduce the OAR doses, as the FSRT plans involved small size radiation fields with sharp dose fall off with FFF beams, thereby saving critical organs and avoiding radiation-induced carcinogenesis. Trying to spare the OARs and preventing the long-term danger of secondary cancer is the goal of using FFF beams, as stated by Kry et al., because of lower out-of-field radiation caused by less electron contamination, collimator scatter, and head leakage.[20].

When we look into the technical parameters like total MU and TT, all created plans showed higher MU from the base plan values, whereas the TT value is very much reduced in 6FFF and 10 FFF plans from the 6FF plan with its significant p-values in 6FFF and 10FFF plans. This is because more MUs are required to provide a uniform dosage distribution when using the FFF beam shape's tiny segments. FFF beams have a high dosage rate delivery feature, which cuts down treatment times. Our research confirms prior study findings that FFF beam designs had greater MU values and lower TT than FF beam plans which avoids any errors due to the immobilization of patients [21-22].

Apart from these dosimetric and delivery efficiency of FFF, there are many other beneficiary properties of FFF, such as that FFF beams possess lower peripheral dose due to their less leaf transmission, photon head scatter and head leakage making it more suitable for small volume tumours, as mentioned in our study [23-24]. Brain metastasis tumours are claimed to be typically spherical, therefore a very steep dosage gradient is required to protect healthy brain tissue from overexposure [25]. In addition, the FFF beam has a lower integral dosage at the same depth in the periphery compared to FF beams [26].

Research shows that out-of-field dosage, of which the FFF beam has less than the FF beam, is directly responsible for 66% of second malignancies following childhood cancer occurring at the treatment field boundary, which is no more than 5cm outside the edge [27]. We focused on cases where the field size was smaller at the brain region and the depth was shallower since these factors affect the FFF beam's ability to reduce the out-of-field dose. Due to the observed reduction in out-of-field dose with medium and higher energy FFF beams, being more visible at very close to and far from the treatment field edge, we included the 10MV energy in our study on the theory that the time advantage of FFF beam is dose-dependent. [28]. This is because when the flattening filter is pulled out, the collimator scatter is reduced, and at farther distances, there will be lesser head leakage, but the area in between gets a higher dose because an unflattened photon beam has lesser average energy, which increases the patient scatter. A major uniqueness in our study is the selection of Rapid arc technology for our brain metastases FSRT plans as the FFF beams delivers time-efficient treatments primarily when used with VMAT technology as it delivers the treatment with lesser monitor units and treatment time when compared to IMRT [29-30].

In addition to all of these benefits, there are encouraging findings on FFF indicating the beam

enables effective treatment delivery since the lack of FF avoids the primary photon beam attenuation, requiring a less target current to provide the same dosage.[31]. Ines et al. revealed that using FFF beams efficiently reduces tumour cell survival, which can benefit in higher dose Stereotactic Body Radiation Therapy (SBRT) treatments [32].

Our study concludes that FFF overweighs the FF in all aspects of plan quality, dosimetric properties, and delivery efficiency compared to FF in the case of both 6MV and 10MV energies. However, 10MV is always limited owing to the possibility of photoneutron generation and absorbed dosage in patients at beams $\geq$ 10MV and the need for larger MUs for FFF beams where 10MV FFF beams produce more photoneutrons per electron than 10MV beams [33-35]. So, the present study recommends 6FFF as the ideal beam for FSRT treatment of BM in overall basis.

Conclusion

Our study results says that linac-based FSRT delivery of BM using 6FFF results in better dosimetric indices, OAR sparing, shorter treatment time and better plan verification results which in turn improves treatment quality, patient comfort and to have a quality workflow in radiotherapy treatment. For higher treatment modalities such as Rapid arc, the FFF modality has made a significant contribution in decreasing out-of-field dosage and peripheral radiation, especially for situations like brain metastases with smaller fields and shallower depths. Moreover, it has the benefit of fast treatment delivery and energy conservation.

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